Paper No. 30

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte JOHN B. HARLEY

Appeal No. 2001-1263
Application No. 08/475,955

HEARD: April 11, 2002

Before WILLIAM F. SMITH, SCHEINER, and MILLS Administrative Patent Judges.

WILLIAM F. SMITH, Administrative Patent Judge.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the final rejection of claims 1, 2, 5 and 7 through 11. Claims 3, 4, and 6 are pending but are stated in the final Office action (Paper No. 12) to have been withdrawn from consideration by the examiner. These are all the claims pending in the application.

Claims 1, 7, 8, and 9 are representative of the subject matter on appeal and read as follows:[1]

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[1] Due to a restriction requirement, it appears that the subject matter of claim 1 has only been examined to the extent it recites the La/SSB epitopes. See Paper No. 9, page 4.

1. (twice amended) A linear epitope for a human autoantibody selected from the group of peptides of less than forty amino acids comprising an amino acid sequence capable of binding to an autoantibody consisting of

the La/SSB epitopes: QVLNIQMRRTLHKAFKGS (SEQ ID NO:19), NIQMRRTLHKAFK (SEQ ID NO:136), RTLHKAFK (SEQ ID NO:137), ICHQIEYYFGDFNLPRDKFLK (SEQ ID NO:20), YFGDFNLP (SEQ ID NO:138), WVPLEIMIKFNR (SEQ ID NO:21), VPLEIMIK (SEQ ID NO:139), KTKIRRSPSKPL (SEQ ID NO:22), KIRRSPSK (SEQ ID NO:140), NRLNRLTTDFNVIVE (SEQ ID NO:23), NRLNRLTT (SEQ ID NO:118), GEIKWIDFVRGAK (SEQ ID NO:24), KWIDFVRGAK (SEQ ID NO:103), IDFVRGAK (SEQ ID NO:104), SLNKWKSKGRRFKGKGKGNK (SEQ ID NO:25), KSKGRRFK (SEQ ID NO:105), GNLQLRNKEVTW (SEQ ID NO:26), LRNKEVTW (SEQ ID NO:106), IFVVFDSIE (SEQ ID NO:27), FVVFDSIE (SEQ ID NO:107), KETDLLILFKDDYFA (SEQ ID NO:28), ILFKDDYF (SEQ ID NO:108), YKNDVKNRSVYIKGFPT (SEQ ID NO:29), SVYIKGFP (SEQ ID NO:109), TDFNVIVE (SEQ ID NO:110), DFNVIVEA (SEQ ID NO:111), EGIILFKEKAK (SEQ ID NO:31), EGIILFKE (SEQ ID NO:112), KVQFQGKKTKFASD (SEQ ID NO:32), KKTKFASD (SEQ ID NO:113), REDLHILF (SEQ ID NO:33), CLLKFSGD (SEQ ID NO:34), TGPVKRAR (SEQ ID NO:35), KVEAKLRAKQ (SEQ ID NO:36), EAKLRAKQ (SEQ ID NO:114);

the Ro/SSA epitopes: MNRLHRFL (SEQ ID NO:37), LCFGSEGGT (SEQ ID NO:38), CFGSEGGT (SEQ ID NO:115), SEGGTYYIKEQ (SEQ ID NO:39), EGGTYYIKEQ (SEQ ID

NO:141), GTYYIKEQ (SEQ ID NO:142), GTYYI (SEQ ID NO:143), EIKSFSQEGRT (SEQ ID NO:40), KSFSQEGR (SEQ ID NO:144), SQEGRTTKQ (SEQ ID NO:41), GRTTKQEPM (SEQ ID NO:42), STKQAAFKAV (SEQ ID NO:145), ISTKQAAFKAVS (SEQ ID NO:43), KQAAFKAV (SEQ ID NO:146), AFKAVSEVC (SEQ ID NO:44), FTFIQFKKDLKESMK (SEQ ID NO:45), QFKKDLKE (SEQ ID NO:147), SMKCGMWGRA (SEQ ID NO:46), MKCGMWGRA (SEQ ID NO:148), GMWGRALRKAIA (SEQ ID NO:47), GRALRKAI (SEQ ID NO:149), ALAVTKYKQRNGWSHKDLLRLSH (SEQ ID NO:48), TKYKQRNG (SEQ ID NO:150), QRNGWSHK (SEQ ID NO:151), LLRLSHLKPSS (SEQ ID NO:49), RLSHLKPS (SEQ ID NO:152), TKYITKGW (SEQ ID NO:153), ITKGWKEV (SEQ ID NO:154), HELYKEKA (SEQ ID NO:50), LYKEKALSV (SEQ ID NO:51), KALSVETEKLLKYL (SEQ ID NO:52), TEKLLKYL (SEQ ID NO:155), KLLKYLEA (SEQ ID NO:53), LEAVEKVKRTKDE (SEQ ID NO:54), KVKRTKDE (SEQ ID NO:156), HLLTNHLKSKEVWKALLQEMPL (SEQ ID NO:55), LKSKEVWK (SEQ ID NO:157), KSKEVWKA (SEQ ID NO:158), SKEVWK (SEQ ID NO:159), LLRNLGKMTA (SEQ ID NO:56), RNLGKMT (SEQ ID NO:160), LGKMTANS (SEQ ID NO:57), LCNEKLLKKARIHPFHI (SEQ ID NO:58), LLKKARI (SEQ ID NO:161), KKARIHPF (SEQ ID NO:162), TYKTGHGLRGKLKWRPDE (SEQ ID NO:59), YKTGHGL (SEQ ID NO:163), ALDAAFYK (SEQ ID NO:60), AAFYKTFKTVEPTGKRFLLA (SEQ ID NO:61), ASMNQRVLGS (SEQ ID NO:62), EPTGKRFL (SEQ ID NO:164), AMCMVVTR (SEQ ID NO:63), AFSDEMVP (SEQ ID NO:64), VPCPVTTD (SEQ ID NO:65), VLMAMSQI (SEQ ID NO:66), TDCSLPMI (SEQ ID NO:67), LPMIWAQKTNTPA (SEQ ID NO:165), WAQKTNTP

(SEQ ID NO:126), TFAGGVHPAI (SEQ ID NO:69), TFAGGVHP (SEQ ID NO:166), IALREYRKKMDIPAKL (SEQ ID NO:70), REYRKKMD (SEQ ID NO:167);

the Sm B/B' epitopes: IGTFKAFD (SEQ ID NO:168), TFKAFDKH (SEQ ID NO:169), GTFKAFDK (SEQ ID NO:1), TFKAFDKHM (SEQ ID NO:15), DCDEFRKI (SEQ ID NO:170), CDEFAKIK (SEQ ID NO:171), CDEFRKIKPKNAKQP (SEQ ID NO:2), DEFRKJKP (SEQ ID NO:172), EFRKIKPK (SEQ ID NO:173), FRKJKPKN (SEQ ID NO:174), RKIKPKNA (SEQ ID NO:175), KIKPKNAK (SEQ ID NO:176), IKPKNAKQ (SEQ ID NO:177), KPKNAKQP (SEQ ID NO:178), PKNAKQPE (SEQ ID NO:179), EGPPPKDT (SEQ ID NO:16), KDTGIARV (SEQ ID NO:17), RVPLAGAA (SEQ ID NO:3), AGGPGVGRAAGRGVPAG (SEQ ID NO:4), PGVGRAAG (SEQ ID NO:180), IPQAPAGLAG (SEQ ID NO:18), AGLAGPVRGVGGPSQ (SEQ ID NO:5), VRGVGGPS (SEQ ID NO:181), QQVMTPQG (SEQ ID NO:182), QVMTPQGR (SEQ ID NO:183), VMTPQGRG (SEQ ID NO:184), PQGR (SEQ ID NO:128), MTPQGBGT (SEQ ID NO:185), TPQGRGTV (SEQ ID NO:186), PQGRGTVA (SEQ ID NO:187), QGRGTVAA (SEQ ID NO:188), APTQYPPG (SEQ ID NO:189), PTQYPPGR (SEQ ID NO:190), TQYPPGRG (SEQ ID NO:191), QYPPGRGT (SEQ ID NO:192), YPPGRGTP (SEQ ID NO:193), PPGRGTPP (SEQ ID NO:194), PGRGTPPP (SEQ ID NO:195), GRGTPPPP (SEQ ID NO:196), RGTPPPPV (SEQ ID NO:197), GTPPPPVG (SEQ ID NO:198), TPPPPVGRATPPPGI (SEQ ID NO:8), PPPPVGRA (SEQ ID NO:199), PPPGIMAP (SEQ ID NO:9), IMAPPPGM (SEQ ID NO:200), MAPPPGMRPPM (SEQ ID NO:10), MAPPPGMR (SEQ ID NO:201), PPPGMR (SEQ ID NO:125), APPPGMRP (SEQ ID NO:202), PPPGMRPP (SEQ ID NO:123), PPGMRPPM (SEQ ID NO:203),

PIGLPPARGTPIGMPP (SEQ ID NO:11), PPARGTPI (SEQ ID NO:204), PIGMPPPG (SEQ ID NO:12), IGMPPPGM (SEQ ID NO:205), GMPPPGMB (SEQ ID NO:206), PPPGMB (SEQ ID NO:207), MPPPGMRP (SEQ ID NO:208), PPPGMRPP (SEQ ID NO:123), PPGMRPPP (SEQ ID NO:209), MRPPPPGI (SEQ ID NO:210), RPPPPGIR (SEQ ID NO:211), RPPPPGIRGPP (SEQ ID NO:13), PPPGIR (SEQ ID NO:212), PPPPGIRG (SEQ ID NO:213), PPPGIRGP (SEQ ID NO:127), PPGIRGPP (SEQ ID NO:214), RGPPPPGM (SEQ ID NO:215), RGPPPPGMRPPR (SEQ ID NO:14),GPPPPGMR (SEQ ID NO:216), PPPPGMRP (SEQ ID NO:217), PPPGMRPP (SEQ ID NO:123), PPPGMR (SEQ ID NO:125), and PPGMRPPR (SEQ ID NO:218).

7. The epitopes of claim 1 in combination with a pharmaceutical carrier for administration to a patient.

8. The epitopes of claim 7 in an effective concentration for administration to a patient to neutralize circulating autoantibody.

9. The epitopes of claim 7 further comprising a pharmaceutical carrier for administration to a patient, wherein the carrier and concentration of sequences elicit an immune response when administered to a host.

The references relied upon by the examiner are:

Colman, "Effects of amino acid sequence changes on antibody-antigen interaction." Research in Immunology, Vol. 145, pages 33-36, 1994.

Wraith et al. (Wraith), "Antigen recognition in autoimmune encephalomyelitis and the potential for peptide-mediated immunotherapy." Cell, Vol. 59, pages 247-255, 1989.

Tisch et al. (Tisch), "Antigen specific immunotherapy: is it a real possibility to combat T-cell-mediated autoimmunity?" Proc. Natl. Acad. Sci. USA, Volume 91, pages 437-38, 1994.

Kaliyuperumal et al. (Kaliyuperumal), "Nucleosomal peptide epitopes for nephritis-inducing T helper cell of murine lupus. J. Exp. Med., Vol. 183, pages 2459-69, 1996.

The claims stand rejected as follows:

I. claims 7 through 9 under 35 U.S.C. § 112, first paragraph, as being non-enabled,

II. claims 1, 2, 5, 10, and 11 under 35 U.S.C. § 112, first paragraph as being non-enabled,

III. claims 7 through 11 under 35 U.S.C. § 112, second paragraph, as being indefinite, and,

IV. claims 1, 2, 5, and 7 through 11 under 35 U.S.C. 112, second paragraph, as being indefinite.

We reverse all rejections.

DISCUSSION

Rejection I

As seen, claims 7-9 are directed to compositions which comprise the epitopes of claim 1 with a pharmaceutical carrier for administration to a patient. Claim 7 requires that the epitopes be in an effective concentration for administration to a patient to neutralize circulating autoantibody while claim 9 requires that the pharmaceutical carrier and concentration of sequences elicit an immune response when administered to a host. The examiner's reasoning in regard to this rejection is summarized at Page 4 of the Answer where the examiner states "appellant has not disclosed how to use the claimed polypeptides to treat autoimmune patients which are reactive to the La/SSB epitopes. There is insufficient evidence of the invention with respect to the in vivo

predictability of the claimed peptides to use Appellant's invention." In support of this rejection, the examiner relies upon Wraith, Tisch, and Kaliyuperumal.

We have considered the evidence relied upon by the examiner but do not find that it supports a conclusion that claims 7 through 9 are non-enabled.

Turning to Wraith, the examiner states at page 4 of the Answer that Wraith teaches "Inhibition of the response restricted by one class II molecule may lead only to the escape to an autoimmune response to a separate epitope restricted by a different class II molecule." (Page 253, column 1). However, the entire passage from which the examiner extracted the quote from Wraith reads as follows:

> Several potential difficulties are apparent in using MHC "blocking: peptides to treat autoimmune disease. First, peptides are small and would be expected to be rapidly cleared from the circulation. An effective strategy may therefore require the use of slow-release systems or frequent injection schedules. Second, some autoantigens have multiple distinct epitopes that are presented by different class II molecules of the MHC (Zamvil et al., 1988). Inhibition of the response restricted by one class II molecule may lead only to the escape to an autoimmune response to a separate epitope restricted by a different class II molecule. Third, Ac1-11[3A,4A] may be itself immunogenic in mice. Administration of such a peptide could induce a "bystander" Th cell response that, rather than blocking recognition of a self-peptide, could increase the overall T cell response to the self-antigen by recruiting cells specific for subdominant epitopes. This drawback would be overcome by using I-A^u binding peptides of self-proteins to which the animal would normally be tolerant.

As seen, the examiner has cropped the quote and has not considered the document in its entirety. At best, the concern expressed by Wraith relied upon by the examiner is "only a potential difficulty." What the examiner has ignored on this record is the conclusion of Wraith set forth in the last sentence of the article "[b]ased on these properties we have been able to demonstrate the feasibility of immune intervention in an

autoimmune disease through the use of a synthetic peptide." Thus, we do not see that Wraith read in its entirety aids the examiner's case.

We reach the same conclusion in regard to the examiner's reliance upon Tisch. The examiner has relied upon a very limited portion of the document and does not appear to have considered the document as a whole. Tisch only states that it is possible that administering an antigen/peptide after pathogenic T cells have been activated may have an immunizing effect and exacerbate the disease condition. The examiner has not explained why this potential difficulty necessarily leads to a conclusion that claims 7 through 9 are non-enabled. It is not unusual for pharmaceutical compositions to have attendant side affects or not work in their intended manner for every patient. We do not find the portion of Tisch relied upon by the examiner in and of itself establishes that claims 7 through 9 are non-enabled.

Finally, we reach the same conclusion in regard to the examiner's reliance on Kaliyaperumal. As understood, the examiner relies upon that portion of Kaliyaperumal which indicates that peptide autoepitopes when administered to lupus mice in vivo induce the development of severe lupus nephritis. However, the examiner has not favored the record with any analysis as to the nature of the peptide autoepitopes administered in Kaliyaperumal and those which have been examined on the merits in this application. Absent a more fact-based explanation as to the relevance of the reference, we do not find that it establishes a case of non-enablement.

Rejection II

We also reverse the examiner's enablement rejection of claims 1, 2, 5, 10, and 11. As seen from claim 1 on appeal, the claimed linear epitopes are defined in two

significant respects. First, the linear epitope must be a peptide of less than 40 amino acids. Those 39 amino acids then can comprise an amino acid sequence capable of binding to an autoantibody consisting of the specified La/SSB epitopes.

The examiner's concern in this rejection is that "there is no specific disclosure as to what those additional amino acids will to do [sic] antibody binding." Examiner's Answer, page 6. The examiner relies upon Colman for its disclosure that single amino acid change can "dramatically effect antigen-antibody dynamics." Id.

If we understand the examiner's position, it is that it would require undue experimentation in order to determine which peptides as defined in claim 1 on appeal possess the required binding property. The question of undue experimentation was discussed in PPG Indus., Inc. v. Guardian Indus. Corp., 75 F.3d 1558, 1564, 37 USPQ2d 1618, 1623 (Fed. Cir. 1996) as follows:

> In unpredictable art areas, this court has refused to find broad generic claims enabled by specifications that demonstrate the enablement of only one or a few embodiments and do not demonstrate with reasonable specificity how to make and use other potential embodiments across the full scope of the claim. See, e.g., In re Goodman, 11 F.3d 1046, 1050-52, 29 USPQ2d 2010, 2013-15 (Fed. Cir. 1993); Amgen, Inc. v. Chugai Pharmaceutical Co., 927 F.2d. 1200, 1212-14, 18 USPQ2d 1016, 1026-28 (Fed. Cir.), cert. denied, 502 U.S. 856 (1991); In re Vaeck, 947 F.2d at 496, 20 USPQ2d at 1445. Enablement is lacking in those cases, the court has explained, because the undescribed embodiments cannot be made, based on the disclosure in the specification, without undue experimentation. But the question of undue experimentation is a matter of degree. The fact that some experimentation is necessary does not preclude enablement; what is required is that the amount of experimentation "must not be unduly extensive." Atlas Powder Co., v. E.I. DuPont De Nemours & Co., 750 F.2d 1569, 1576, 224 USPQ 409, 413 (Fed. Cir. 1984). The Patent and Trademark Office Board of Appeals summarized the point well when it stated:
>
> > The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a

> reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed.
>
> Ex parte Jackson, 217 USPQ 804, 807 (1982).

The examiner has not performed sufficient fact-finding under the appropriate legal standard in order to properly arrive at the conclusion that practicing the claimed invention would require undue experimentation. It may be that determining which of the myriad peptides encompassed by claim 1 on appeal possess the requisite binding property will involve further experimentation. But that does not mean that the claim is non-enabled. Absent further fact-finding and analysis by the examiner as to why the amount of experimentation needed in order to make the determination would be considered undue rather than routine, we do not find the examiner has established a prima facie case of non-enablement.

Rejection III

We reverse the examiner's rejection of claims 7-11 under 35 U.S.C. § 112, second paragraph. As stated at Page 7 of the Examiner's Answer, "[c]laim 1 is a product claim, limited to a peptide of upto [sic] 39 amino acids. Claims 7-11 have an additional pharmaceutical carrier, labels or are immobilized onto substrate, thereby broadening the claim to be a composition claim." To the extent that we understand the examiner's position, we do not find that these claims are in violation of the definiteness requirement of § 112, second paragraph.

If the examiner believes that dependent claims 7 through 11 are improper dependent claims, the rejection would be based upon paragraph 4 of § 112, not

paragraph 2. The examiner has not explained why one of ordinary skill in the art would have any difficulty in determining the metes and bounds of claims 7 through 11. Absent such an explanation from the examiner, we do not find that claims 7-11 are indefinite.

Rejection IV

Finally, we reverse the examiner's rejection of claims 1, 2, 5, and 7 through 11 under 35 U.S.C. § 112, second paragraph.

As explained at page 7 of the Examiner's Answer, the examiner is concerned that:

> Amended claim 1 is unclear. If Appellant wants to claim a peptide up to 40 amino acids wherein said peptide comprises the disclosed SEQ ID No.s, the claim should be read as "A linear peptide epitope for a human autoantibody consisting of less than forty amino acids, wherein said peptide epitope comprises an amino acid sequence capable of binding to an autoantibody and is selected from the group consisting of ...".

Again, the examiner has not explained why one of ordinary skill in the art would have any difficulty ascertaining the metes and bounds of the claims on appeal. As set forth above, claim 1 as directed to linear epitopes for a human autoantibody. The epitope must first be a peptide of less than 40 amino acids. Second, the peptide must comprise an amino acid sequence capable of binding to an autoantibody consisting of the listed La/SSB epitopes. We find nothing inconsistent or confusing with the use of the term "comprising" in claim 1. Again, the claimed peptide first must be less than 40 amino acids and consist of one of the sequences set forth in the SEQ ID Nos. specified in the claim. Apart from those two requirements, the peptide may "comprise" other amino acids as long as the resulting peptides possess the required binding property.

The examiner's decision is reversed.

REVERSED

William F. Smith Administrative Patent Judge	)
Toni R. Scheiner Administrative Patent Judge	) BOARD OF PATENT) APPEALS AND) INTERFERENCES
Demetra J. Mills Administrative Patent Judge	)

ELD

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